

Effect of Dietary Fat on Length of the Follicular Phase of the Menstrual Cycle in a Controlled Diet Setting

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ABSTRACT. The length of the follicular phase of the menstrual cycle (defined as the time from the first day of menses until the day of urinary LH peak, inclusive) was examined in 30 healthy, premenopausal women. The women consumed defined, weight maintaining diets, with a ratio of polyunsaturated to saturated fatty acids (P/S ratio) of either 0.3 or 1.0. Both P/S groups consumed a high fat diet (40% energy from fat) for 4

menstrual cycles, followed by 4 menstrual cycles of a low fat diet (20% energy from fat). There was a significant increase ($P < 0.006$) in the length of the follicular phase of the menstrual cycle during consumption of the low fat diet. Two thirds of the women showed increases in follicular phase length with an average increase of 1.9 days. (*J Clin Endocrinol Metab* 74: 1171-1175, 1992)

ALTHOUGH not extensively studied, a variety of dietary practices, including caloric restriction, vegetarian or meatless diets, and reduction of percent calories coming from fat, have been shown to affect the menstrual cycle. Studies reported in the literature differ widely in design, self-selected diets of participants, and dietary modifications. It is therefore difficult to draw firm unifying conclusions regarding both specific nutrients which affect the menstrual cycle, and the possible mechanisms involved.

Most women develop amenorrhea when weight loss results in a decrease of more than 13% of ideal body weight (1), and even relatively small reductions in weight may impair fertility (2). In several studies of caloric restriction, increases in menstrual cycle irregularities (insufficient luteal phase determined by length and/or progesterone levels, altered episodic LH secretion during the follicular phase, etc.) were found when women were younger, lost more weight, or were on meatless diets (3-5). The duration of these studies, however, was generally too short (one menstrual cycle to 6 weeks) to detect changes in follicular phase length. It is unclear how dietary changes related to weight loss in these studies correlate with changes in fat or other specific nutrients.

In a study of a population of runners, most amenor-

rheic women (9/11) were vegetarians and also consumed significantly less fat than the menstruating runners (6). Hill *et al.* (7, 8), in studies conducted in South Africa, found that largely vegetarian black women, placed on a meat-containing diet, experienced a significantly increased follicular length, while meat-consuming caucasian women, placed on a meatless diet, showed a shorter follicular phase. The percentage of calories derived from fat was maintained at an approximately constant level.

In the studies described above, most or all of the food items consumed were self-selected. The only controlled diet study, published to date, which involved a reduction in fat as a percentage of calories and reported on menstrual cycle length, showed no differences (9). However the study encompassed only 1 complete menstrual cycle and involved 6 women. In the analysis described here 30 women each consumed a low fat (20% energy from fat) and a high fat (40% energy from fat) diet for a period of 4 menstrual cycles each. A spectrum of hormonal, lipid, and bile acid analytes were measured. A previous report on this study documents a significant increase in cycle length and in menses length while on the low fat diet, based on self report (10). Here, we use urinary LH data to determine effects on the follicular phase length biochemically.

Materials and Methods

Study subjects

Thirty one healthy, premenopausal women, aged 20-40 yr completed a diet study lasting nine menstrual cycles. The study

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addressed the effects of consumption of a high fat (40% energy from fat) as compared with a low fat (20% energy from fat) diet, at either low (0.3), or high (1.0) ratios of polyunsaturated to saturated fatty acids (P/S). Screening of volunteers eliminated women with health problems, use of oral contraceptives the year before the study, regular use of medications, self-reported menstrual irregularities, or other reproductive problems, pregnancy or breast feeding within the year before the study, and dietary patterns incompatible with the study. Women whose weights were less than 90%, or greater than 120%, of the 1983 Metropolitan Life Insurance Table were excluded. Of the 37 women who passed screening evaluations and began the study, 31 completed the study. One woman was eliminated from the analyses reported here due to difficulty in establishing the day of the LH peak in 1 menstrual cycle. The study was approved by the Institutional Review Boards of the NIH and Georgetown University School of Medicine.

Experimental design

After a free-living baseline period of one menstrual cycle, each woman was placed on a high fat diet for four menstrual cycles. This was followed by four menstrual cycles on a low fat diet. The women were randomized to one of two P/S groups (P/S ratio = 0.3 or 1.0) which were maintained throughout both the high and low fat dietary periods. Randomization to P/S ratio groups was based largely on weight and height, and ensured that the few smokers in the study ($n = 7$) were distributed between the two P/S groups as equally as possible. Randomization was accomplished by stratifying according to smoking status. Within each strata subjects were ranked by weight/height. A coin toss determined which P/S ratio women with odd-numbered ranks would consume, and women with even numbered ranks were assigned to the other P/S group. Data on age, height, and weight have been previously published (11). Although subjects were not randomized on age no significant differences in age were found between the two groups (11).

Diets were formulated from commonly available foods in a 14 day repeating menu cycle. Diets were analyzed using United States Department of Agriculture Handbook 8 (12). Menus for four caloric intake levels were designed: 1600, 2000, 2400, and

2800 kcal. Weight was maintained as close to constant as possible during the course of this study. In order to maintain body weight, whenever a woman gained or lost at least 1 kg and maintained this weight change for at least 3 days, she was moved from one caloric level to another. Women were weighed daily before breakfast. In reducing the energy intake from fat, the energy from protein was maintained at about 16–17%, whereas that from carbohydrate was increased. No vitamin or mineral supplements or alcohol were consumed while on the study. Meat was present in both high and low fat diets an average of twice per day and fish and poultry were present an average of once a day. Meals were prepared in the Beltsville Human Nutrition Research Center (BHNRC). On weekdays, morning and evening meals were eaten in the BHNRC dining facility and a carry-out lunch was provided. Weekend meals were packaged for home consumption. The mean daily dietary intake for the two P/S groups during the baseline, high fat, and low fat periods is shown in Table 1 (10).

Hormone assays

Twenty-four hour urine collections were obtained from study participants from day 6 through day 27 of the last menstrual cycle of each dietary period. LH assays were performed by Maryland Medical Laboratory, Inc. using the Amersham Amersham-M LH RIA Kit (Arlington Heights, IL). All analyses were performed in duplicate. Intra- and interassay variability for LH were 6.2% and 11.8%, respectively, at an average LH level of 82.2 IU/L, and 11.2% and 18.7% at an average LH level of 15.8 IU/L. To the extent possible assays were performed in the same run. For each subject, assays were performed on specimens for sequential days centered on an estimated ovulation day, based on the subject's reported menstrual history, until the day of LH peak could be established. An average of 7.0 days were assayed per cycle. For 59 of the 60 LH peaks established values were also obtained for at least 1 day preceding and 1 day after the LH surge. In one case no data was available after the peak.

Statistical analyses

Comparisons of the length of the follicular phase of the menstrual cycle on high and low fat diets were made by Stu-

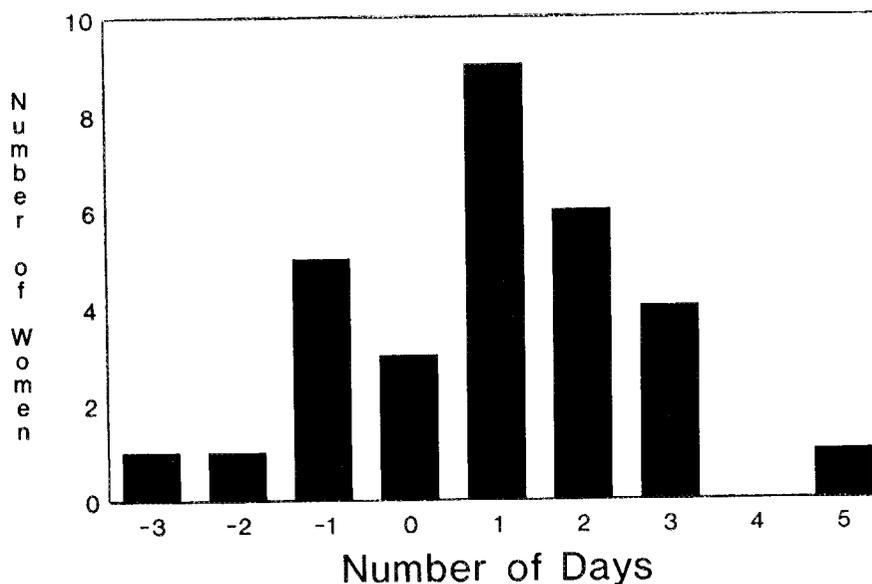
TABLE 1. Daily nutrient intakes for subjects in both P/S groups during baseline, high and low fat dietary periods (means with SE in parenthesis)

	Baseline (freeliving)	Controlled dietary periods (% energy from fat)			
		40% P/S ratio		20% P/S ratio	
		0.3	1.0	0.3	1.0
No. of subjects	31	15	16	15	16
Energy, kJ	8620 (343)	9530 (272)	9130 (339)	9450 (406)	9240 (460)
Energy, kcal	2060 (82)	2280 (65)	2180 (81)	2260 (97)	2210 (110)
Protein, % energy	14	16	16	17	17
Carbohydrate, % energy	47	45	45	64	64
Fat, % energy (g) ^a	39 (89.3)	39 (98.8)	39 (94.5)	19 (47.7)	19 (46.7)
Saturated fat, g	32.7 (1.7)	44.2 (1.3)	26.8 (1.1)	20.9 (0.7)	12.3 (0.6)
Oleic acid, g	31.5 (1.5)	30.5 (0.9)	33.5 (1.4)	14.9 (0.6)	17.0 (0.8)
Linoleic acid, g	14.1 (1.0)	14.6 (0.4)	26.1 (0.9)	6.9 (0.2)	12.9 (0.6)
Crude fiber, g	3.3 (0.3)	5.8 (0.2)	5.6 (0.2)	7.9 (0.2)	7.7 (0.3)

^a Fat given in % energy and in grams.

Change in Length of Follicular Phase Low Fat Diet - High Fat Diet

FIG. 1. The change in length of the follicular phase of the menstrual cycle: low fat diet minus high fat diet. For each study participant the length of the follicular phase while consuming the high fat diet was subtracted from the length of the follicular phase while consuming the low fat diet. 0 = No change in length, 1 = follicular phase during low fat diet cycle was one day longer than during high fat diet cycle, etc.



dent's *t* tests for paired data and by Wilcoxon's signed rank tests for paired data, with each subject serving as her own control. Results of these tests were very similar and only data from the Student's *t* test for paired values are shown. Group comparisons of differences in the length of the follicular phase of the menstrual cycle between individuals consuming different P/S diets while consuming either high or low fat diets were made by Student's *t* test. Statistical analyses were performed using the Statistical Analysis System, SAS (13).

Results

The follicular phase of the menstrual cycle was defined as the time from the first day of menses until the day of LH peak, inclusive. Figure 1 shows, for each woman in the study, the change in length of the follicular phase of the menstrual cycle. This was computed by subtracting the length of the follicular phase while consuming a high fat diet from the length while consuming a low fat diet. A significant increase ($P < 0.006$) in length of the follicular phase was observed when women consumed low fat, as compared to high fat diets. Of the 30 women studied, 3 showed no change in length of the follicular phase, 7 showed a shortening of the follicular phase, and 20 women showed an increase in follicular phase length. For the 20 women with increases in length of the follicular phase the average increase was 1.9 days. For all 30 women the average change in the length of the follicular phase was an increase of 0.9 days.

The difference in follicular phase length was further

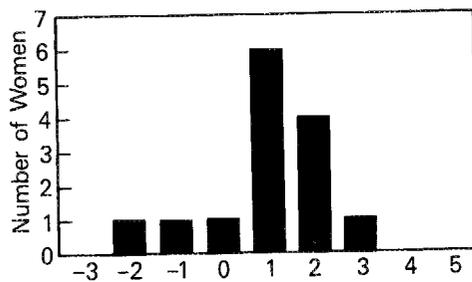
examined with respect to the P/S ratios of the diets (Fig. 2). The percentage of women who experienced a decrease, no change, or an increase in follicular phase length was 14, 7, and 79, respectively, for women who consumed diets with a P/S ratio of 0.3, and 31, 13, and 56, respectively, for women who consumed diets with a P/S ratio of 1.0. The average increase in length of the follicular phase was 1.0 day ($P < 0.01$) for women who consumed diets with a P/S ratio of 0.3, and 0.9 days ($P < 0.11$) for women who consumed diets with a P/S ratio of 1.0. It should be noted that the number of women in each P/S ratio group is fairly small.

Comparisons of follicular phase length were made between the groups of women who consumed diets with P/S ratios of 1.0 and 0.3. No significant differences were observed while either a high fat or a low fat diet was being consumed. However sample sizes are fairly small.

Discussion

The data presented here describe biochemical evidence for a significant increase in the length of the follicular phase of the menstrual cycle on a low fat *vs.* a high fat controlled diet regimen. The only other similarly controlled diet study in the literature that dealt with cycle length reported no change (9). However that study involved only six women and a much shorter time on each diet, one *vs.* four menstrual cycles. Existent effects may not have been observable under the conditions of the

Change in Length of Follicular Phase Low Fat Diet — High Fat Diet P/S = 0.3 N = 14



P/S = 1.0 N = 16

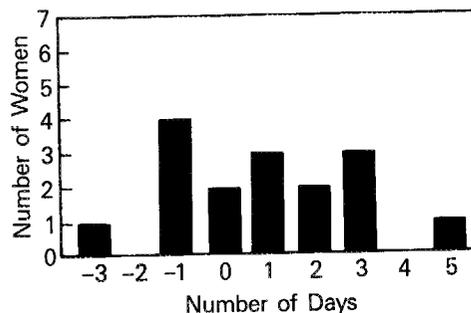


FIG. 2. The change in length of the follicular phase of the menstrual cycle: low fat diet minus high fat diet for women consuming a diet with P/S ratio = 0.3 (top) or with P/S ratio = 1.0 (bottom).

shorter study.

It is difficult to compare the results of studies dealing with weight loss regimens, supplements, or vegetarian *vs.* meat containing diets with those reported here. For instance, the dietary regimens of the study reported by Hill *et al.* (7, 8) and that described here differ substantially. In the study described here both diets contained substantial amounts of meat, and all foods were prepared and supplied by the study. In the study described by Hill *et al.* (7, 8) the different diets consumed were relatively constant in the percent energy from fat. Also the women who participated were either responsible for obtaining their own meals, with menus provided to the subjects and compliance documented by 3-day food records, or a supplemental meal was given to the women. Many studies of weight reduction diets which addressed changes in the menstrual cycle were of short duration (3–5). They frequently started with the first day of menses and thus may not have shown effects in the follicular phase. However, when all study designs are considered it does appear that there may be effects of meat consumption on the menstrual cycle distinct from overall differences in fat consumption. Further studies dealing with both quantity and sources of fat are needed to clarify these

relationships.

The length of the follicular phase of the menstrual cycle is significantly influenced by age, decreasing throughout reproductive life, as does the length of the entire menstrual cycle, until just before menopause (14–16). A change in menstrual cycle length of 1 day has been shown to generally reflect a change in follicular phase length of 0.77 days, and in luteal length of 0.23 days (17). A number of breast cancer risk factors, including age at menarche and menopause, age at first birth, parity, *etc.* (18–21) appear to be related to total exposure to estrogens and total lifetime menstrual activity. Exposure to estrogens may vary with cycle length.

The literature on cycle length and breast cancer is somewhat inconsistent. Whereas several studies, prospective and case-control, find no association between cycle length and breast cancer (22, 23), Olsson *et al.* (24, 25) showed in a case-control study that, after correction for age, breast cancer patients reported significantly shorter cycles than benign breast disease patients or controls. Yuan *et al.* (26), in a case-control study conducted in Shanghai, China, also report significantly increased risk of breast cancer when cycles were less than 25 days in length. The association between dietary fat and breast cancer is also controversial. Whereas animal studies (27), ecological, and migrant studies offer strong support for an association, analytic epidemiologic studies, both case-control and prospective, have had inconsistent results (28, 29). A relation between dietary fat and breast cancer could be mediated by the influence of dietary fat on endogenous hormone levels. Several studies involving hormone measurements on individuals before and after changes in dietary fat level have shown decreases in circulating levels of one or more of the following: total estradiol (30–33), estrone (30, 31), estrone sulfate (34), and weakly bound estradiol (33), to accompany adherence to a low fat diet. In some cases the change to a lower level of dietary fat was accompanied by other dietary changes, including increased dietary fiber levels, which might also effect endogenous hormones (30, 32, 34).

The underlying mechanisms which result in menstrual cycles of differing length are unclear, as is the extent to which cycles of different length can be influenced by diet. The relationships between cycle length and breast cancer, and between diet and cycle length, form an intricate network. It is possible that metabolic studies such as that described here, may ultimately shed light on breast cancer etiology, and offer some possibilities for prevention.

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